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How Microbes Evolve to Dodge the Membrane Disruptive Actions of Antimicrobial Peptides

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Antimicrobial peptides (AMPs) kill bacteria by forming pores that increase membrane permeability to ions or larger molecules. It has been proposed that AMPs selectively disrupts microbial membranes over mammalian membranes. The question remains as to why microbes have not been more successful in resisting the activity of AMPs. As the target of antimicrobial peptides is the plasma membrane, a microbe would have to redesign its membrane, changing the composition and/or organization of its lipids to dodge the action of AMPs. This is likely to be a 'costly' solution for most microbial species. Yet, over the years, some pathogens have successfully developed countermeasures to limit the effectiveness of AMPs, allowing them to survive in the presence of AMPs that would have otherwise killed them. Here we explore the factors involved in antimicrobial resistance. To get at the mechanism of action of AMPs, we directly visualize the topological changes induced by AMPs in model membranes via atomic force microscopy (AFM). AMPs induce structural transformations in supported lipid bilayers, progressing from fingerlike instabilities at bilayer edges, to the formation of surface-defects, and finally to a network of stripe-like structures in zwitterionic model membranes with increasing PG-1 concentration. While zwitterionic bilayers exhibit surface defects with the addition of AMPs, surface defects are not observed as an intermediate stage of membrane disruption in anionic lipid membranes. These and other results obtained from lipids with different chain length indicate that lipid compositions, lipid fluidity and hydrophobic mismatch between AMPs and acyl chains of the lipid bilayer all play important roles in antimicrobial resistance.